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# 东川乌头中一个新的去甲二萜生物碱

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**摘要：从东川乌头（*Aconitum geniculatum* Fletcher et Lauener）块根的乙醇提取物中分离得到3个去甲二萜生物碱，经1D、2D－NMR技术鉴定，分别为20－乙基－8－乙酰氧基－14－（对－羟基苯甲酰氧基）－1α，6α，16β，18－四甲氧基乌头烷－3α，13β二醇（1）、20－乙基－8－乙酰氧基－14－苯酯基乌头烷－3α，13β二醇（2）和20－乙基－8－乙酰氧基－14－（对－甲氧基苯酯基）乌头烷－3α，13β二醇（3），其中1为新化合物，命名为滇羟碱（geniculine）。**

**关键词：东川乌头；去甲二萜生物碱；滇羟碱**
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# A New Norditerpenoid Alkaloid from *Aconitum geniculatum*

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**Abstract**：Geniculine 1，a new norditerpenoid alkaloid，was isolated from the root of *Aconitum geniculatum* Fletcher et Lauener（Ranunculaceae）. Its structure was elucidated as 20－ethyl－8－acetoxy－14－（*p*－hydroxybenzoyloxy）－1α，6α，16β，18－tetramethoxyaconitane－3α，13β－diol mainly by 1D and 2D NMR techniques.

**Key words**：*Aconitum geniculatum*；Norditerpenoid alkaloids；Geniculine

There is a long and fascinating history to use the plants in *Aconitum* and *Delphinium*，which are rich in biologically active norditerpenoid alkaloids for many purposes（Ding，1989）. *Aconitum geniculatum* Fletcher et Lauener，a folk medicine，is distributed over Dongchuan area of Yunnan Province in China. The isolation and structure elucidation of seven norditerpenoid alkaloids from this species were reported in a previous paper（Hao，1985）. Continued investigation on the constituents of this species has resulted in the isolation of a new norditerpenoid alkaloid named geniculine 1 along with two known ones，indaconitine 2 and yunaconitine 3，from the ethanolic extracts of the roots. This is the first report on the occurrence of *p*－hydroxybenzoyloxy group of diterpene alkaloids in ranunculaceoous plants.

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## Results and Discussing

Geniculine 1, $[\alpha]_D^{25.5} + 31.6°$ (c, 0.00372, $CHCl_3$), was obtained as amorphous powder and the molecular formula of $C_{34}H_{47}NO_{11}$ was determined by EIMS and combined with its $^{13}$C NMR data. The IR spectrum indicated the presence of hydroxyl groups (3450cm$^{-1}$) and carbonyl (1730 and 1710cm$^{-1}$) groups, $^1$H NMR spectrum revealed the presence of four methoxyl groups (δ 3.11, 3.20, 3.26 and 3.50, each 3H, s), an acetyl group (δ 1.30, 3H, s) and an ethylamino group (δ 1.05, 3H, t, J = 7.2Hz). The analysis of EIMS and NMR including HMBC spectra led to a conclusion that geniculine must have a p – hydroxybenzoyloxy group at C – 14. Mass spectrum showed a base peak at m/z 121 corresponding to the fragmentation of the *p* – hydroxybenzoyl group in the molecule. The aromatic protons of the *p* – hydroxybenzoyl group were evident from the signals at ( 7.90 and 6.81 (2H each, d, J = 9Hz, Ar – H) and 3.94 (1H, s, 4′ – OH). Long – range correlation (Fig. 1) between the hydroxyl signal (δ 3.94, s) and the aromatic carbon signals at ( 115.4 and 161.3 suggested that the hydroxyl group was located at C – 4′. The $^1$H and $^{13}$C spectra were similar to those of known alkaloids 2 and 3 except for the difference due to different substituents at the C – 4′. When the substitution group at C – 4′ changed from a methoxyl to a hydroxyl, the chemical shift of C – 4′ (δ 161.3) was upfield shifted by 2.2 ppm from that of yunaconitine (δ 163.5). The adjacent C – 3′ and C – 5′ carbons at δ 115.4 compared with that of 3 were downfield shifted by about 2 ppm as a result of the β – effect of the C – 4′ hydroxyl group. The structure of 1 was thus assigned to be 20 – ethyl – 8 – acetoxy – 14 – (p – hydroxybenzoyloxy) – 1α, 6α, 16β, 18 – tetramethoxy – aconitane – 3α, 13β – diol.

Indaconitine 2 (Khetwal, 1994) and yunaconitine 3 (Yu, 1993) were identified by IR, MS, 1HNMR and $^{13}$C NMR spectral evidence.

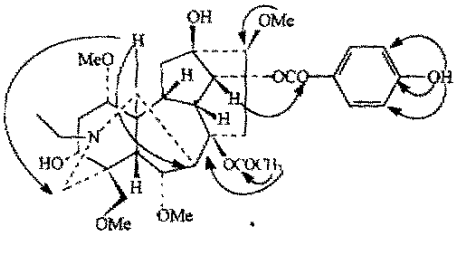


Figure 1. The HMBC correlations of 1

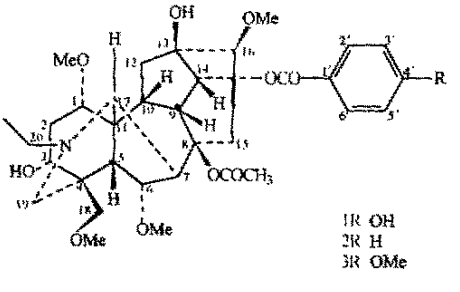


Figure 2. The Structures of 1 – 3

## Experimental

Optional rotations were measured in $CHCl_3$. IR spectra were recorded on a IR – 408 spectrometer. NMR spectra were determined on a Bruker AM – 400 instruments with TMS as internal standard and $CDCl_3$ as solvent. MS was recorded with a VG AutoSpec – 3000 mass spectrometer.

The roots of *Aconitum geniculatum* Fletcher et Lauener were collected from the Dongchuan area of Yunnan Province, China, in September, 1994. It was identified by Prof. Zhi – Hao HU at Yunnan University. A voucher specimen has been deposited in the Herbarium of Yunnan University.

The shade dried and powdered roots of *A. genicultum* (4.8kg) were soaked with 90% EtOH. The extract was evaporated in vacuum, and the syrup (2000 mL) was dissolved in 5% HCl. The acidic solution was extracted with $CHCl_3$. The $CHCl_3$ extract was discarded. The remaining aqueous acid solutions were basified with concentration $NH_4OH$, adjusted to pH 11. The basified solutions were extracted repeatedly with $CHCl_3$ to give a mixture of crude alkaloid (120g). The crude alkaloid fraction was chromatographed repeatedly over silica gel eluted with petrol – EtOAc – 3% $NEt_3$ and EtOAc – MeOH – 3% $NEt_3$ to yield 1 (8mg), 2 (300mg), 3 (80g).

Table 1 $^{13}C$ NMR data of 1 – 3 (400MHz, $CDCl_3$)

| carbon | 1 | 2 | 3 | carbon | 1 | 2 | 3 |
|---|---|---|---|---|---|---|---|
| 1 | 82.2 (d) | 82.2 (d) | 82.2 (d) | 18 | 77.3 (t) | 76.8 (t) | 76.3 (t) |
| 2 | 33.3 (t) | 33.6 (t) | 33.4 (t) | 19 | 47.6 (t) | 47.3 (t) | 47.3 (t) |
| 3 | 72.0 (d) | 71.3 (d) | 71.6 (d) | N – $\underline{CH_2}CH_3$ | 48.7 (t) | 48.7 (t) | 48.7 (t) |
| 4 | 43.1 (s) | 43.1 (s) | 43.2 (s) | N – $CH_2$ $\underline{CH_3}$ | 13.2 (q) | 13.3 (q) | 13.2 (q) |
| 5 | 40.9 (d) | 40.8 (d) | 40.8 (d) | 1 – OMe | 55.7 (q) | 55.7 (q) | 55.3 (q) |
| 6 | 83.1 (d) | 83.1 (d) | 83.1 (d) | 6 – OMe | 58.0 (q) | 57.7 (q) | 57.3 (q) |
| 7 | 48.7 (d) | 48.7 (d) | 48.8 (d) | 16 – OMe | 58.8 (q) | 58.6 (q) | 58.8 (q) |
| 8 | 85.8 (s) | 85.5 (s) | 85.5 (s) | 18 – OMe | 59.1 (q) | 59.0 (q) | 59.1 (q) |
| 9 | 44.7 (d) | 44.7 (d) | 44.7 (d) | 8 – CO – | 170.2 (s) | 169.6 (s) | 169.9 (s) |
| 10 | 47.3 (d) | 47.3 (d) | 47.5 (d) | $CH_3$ | 21.6 (q) | 21.4 (q) | 21.6 (q) |
| 11 | 50.3 (s) | 50.1 (s) | 50.2 (s) | 14 – CO | 166.3 (s) | 166.2 (s) | 166.5 (s) |
| 12 | 35.2 (t) | 35.2 (t) | 35.2 (t) | 1′ | 121.8 (s) | 130.1 (s) | 122.6 (s) |
| 13 | 74.8 (s) | 74.7 (s) | 74.7 (s) | 2′, 6′ | 131.9 (d) | 129.6 (d) | 131.7 (d) |
| 14 | 78.5 (d) | 78.7 (d) | 78.5 (d) | 3′, 5′ | 115.4 (d) | 128.4 (d) | 113.8 (d) |
| 15 | 39.8 (t) | 39.4 (t) | 39.6 (t) | 4′ | 161.3 (s) | 133.0 (d) | 163.5 (s) |
| 16 | 83.6 (d) | 83.5 (d) | 83.5 (d) | 4′ – OMe | | | 55.4 (q) |
| 17 | 61.7 (d) | 61.5 (d) | 61.7 (d) | | | | |

Geniculine (1), Amorphous powder, $[\alpha]_D^{25.5}$ + 31.59° ($CHCl_3$, c 0.4); EIMS m/z (rel. int.): 585 $(M - CH_3COOH)^+$ (48), 570 $(M - CH_3COOH - CH_3)^+$ (24), 554 $(M - CH_3COOH - OCH_3)^+$ (52), 524 $(M - COC_6H_4OH)^+$ (5), 464 $(M - CH_3COOH - COC_6H_4OH)^+$ (7), 448 $(M - CH_3COOH - OCOC_6H_4OH)^+$ (12), 121 (100). IR (KBr) $cm^{-1}$: 3450, 2900, 1710, 1605, 1508, 1450, 1370, 1280, 1220, 1160, 1090, 850, 770, 720, 695. $^1H$ NMR δ: 1.05 (3H, t, J = 7.2Hz, $NCH_2CH_3$), 1.30 (3H, s, $COCH_3$), 3.50, 3.26, 3.20, 3.11 (each 3H, s, C16, C18, C1, C6 – OMe, respectively), 3.08 (1H, m, H – 1β), 3.78 (1H, dd, J = 4.6, 9.0 Hz, H – 3β), 3.98 (1H, d, J = 6.5 Hz, H – 6β), 4.83 (1H, d, J = 5 Hz, H – 14β), 3.38 (1H, dd, J = 8.8, 5.5 Hz, H – 16), 2.92 (1H, s, H – 17), 3.56, 3.52 (2H, dd, J = 8.9 Hz, H – 18α, H – 18β, respectively), 2.93, 2.34 (2H, m, H – 19α, H – 19β, respectively), 3.94 (1H, s, H – 4′), 7.90, 6.81 (each 2H, d, J = 9 Hz, $COC_6H_4OH$); $^{13}C$NMR see Table 1.

Indaconitine (2), White crystals, mp 167 ~ 169℃. EIMS m/z (rel. int.): 629 $M^+$ (4), 614 $(M - CH_3)^+$ (7), 598 $(M - OCH_3)^+$ (100), 569 $(M - CH_3COOH)^+$ (34), 554 (M –

$CH_3COOH - CH_3$) + (14), 538 ($M - CH_3COOH - OCH_3$)$^+$ (22), 448 (4), 105 (70). IR (KBr) $cm^{-1}$: 3500, 2950, 1715, 1600, 1450, 1370, 1280, 1275, 1230, 1100, and 710. $^1H$ NMR δ: 1.03 (3H, t, J = 7.2 Hz, $NCH_2CH_3$), 1.21 (3H, s, C - 8 - $OCOCH_3$), 3.48, 3.23, 3.18, and 3.09 (each 3H, s, C16, C18, C1, C6 - OMe, respectively), 4.01 (1H, d, J = 6.5 Hz, H - 6β), 3. 40 (1H, dd, J = 8.8, 5.5 Hz, H - 16), 4.84 (1H, d, J = 5 Hz, H - 14β), 8.00 (2H, dd, J = 2.0, 7 Hz, 2′, 6′ - H), 7.50 (1H, dd, J = 7.5, 2.0 Hz, 4′ - H), 7.38 (2H, dd, J = 7.5, 7.0 Hz, 3′, 5′ - H); $^{13}$ CNMR see Table 1.

Yunaconitine (3), White powder, $[\alpha]_D^{25.5}$ + 37.7° ($CHCl_3$, c 0.8); mp: 142 ~ 143℃. EIMS m/z (rel. int.): 659 $M^+$ (2), 628 ($M - OCH_3$)$^+$ (58), 699 ($M - CH_3COOH$)$^+$ (1.3), 135 (100). IR (KBr) $cm^{-1}$: 3500, 2800, 2600, 1730, 1700, 1605, 1510, 1450, 1380, 1280, 1255, 1180, 1100, 1030, 980, 940, 850, 770 and 690. $^1H$ NMR δ: 1.10 (3H, t, J = 7.2Hz, $NCH_2CH_3$), 1.34 (3H, s, $COCH_3$), 3.87, 3.55, 3.30, 3.25, 3.16 (each 3H, s, C4′, C16, C18, C1, C6 - OMe, respectively), 4.03 (1H, d, J = 6.5 Hz, H - 6β), 4.84 (1H, d, J = 5 Hz, H - 14β), 6.93, 8.01 (each 2H, d, J = 9 Hz, $COC_6H_4OH$); $^{13}$ C NMR see Table 1.

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